

REMARKS

Claims 17, 19-20, 23, 27, and 28 are pending in the present application.

Favorable consideration of this application, as presently amended, is respectfully requested.

The rejection of Claims 17 and 23 under 35 U.S.C. §102(b) over Lehmann et al is obviated by amendment.

At the outset, Applicants wish to thank the Examiner for recognizing the “differences between a consensus protein and an ancestral protein.” (paper number 17, page 10) Applicants would also like to thank the Examiner for indicating that Claims 18-22 and 24-26 are free of the art of record. Consistent with this indication, Claim 17 has been amended to incorporate the limitations of Claims 18, 21, and 22, while Claim 23 has been amended to incorporate the limitation of Claims 24-26.

Applicants request withdrawal of this ground of rejection in view of the aforementioned amendments and the indication by the Examiner that the limitations that have been added to Claims 17 and 23 are free of the disclosure of Lehmann et al.

Acknowledgment that this ground of rejection has been withdrawn is requested.

The rejection of Claims 17-26 under 35 U.S.C. §112, first paragraph (“written description”), is obviated in part by amendment and traversed in part.

In making this ground of rejection, the Examiner concludes that the present claims are “directed to a method for improving the thermostability by comparing the amino acid sequence of proteins of different function.” Contrary to this assertion by the Examiner, the definition of “proteins belonging to the same family,” as defined on page 5, line 29 to page 6,

line 6 of the present specification, clearly indicates that this expression includes proteins that are similar to each other in "at least one of the function, amino acid sequence, domain structure, and steric structure." In order to ensure clarity and to specifically indicate the scope of the claimed invention, Claims 17 and 23 have been amended to recite this definition.

Applicants direct the Examiner's attention to MPEP § 2163.02:

An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gostelli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989).

Applicants, refer the Examiner pages 5, line 3 to page 6, line 15 and Example 1 of the present application. These sections of the application provide that "information of amino acid sequences of proteins corresponding to each other ... ". Moreover, it is apparent for those skilled in the art that proteins derived from two or more species correspond each other when these proteins appear at the similar location in the phylogenetic tree designed for each individual species.

As such, in one embodiment of the present invention, maximum parsimony method or maximal likelihood method is used for preparing a phylogenetic tree (see page 6, line 26 to page 8, line 14). Accordingly, Claims 17 and 23 have been amended to introduce the limitation of these two methods for preparing a phylogenetic tree. Applicants submit that it is now clear to the skilled artisan that proteins derived from two or more species correspond to each other when these proteins appear at the similar location in the phylogenetic tree designed for each individual species. This fact is also suggested in the specification at page 4, line 20 to page 5, line 2. In addition, the location of the "ancestral protein" in a phylogenetic tree may be found at page 5, lines 10-14, wherein it may be located at the root of the phylogenetic tree.

Therefore, the present claims do allow the skilled artisan to recognize what has been invented and what is claimed is adequately described in the specification within the meaning of 35 U.S.C. § 112, first paragraph.

Accordingly, withdrawal of this ground of rejection is requested.

The rejection of Claims 17-26 under 35 U.S.C. § 112, first paragraph (“enablement”), is traversed.

The Office has taken the position that while the specification is enabled for a method of improving the thermostability of 3-isopropyl malate dehydrogenases wherein amino acid sequences of 3-isopropyl malate dehydrogenases and isocitrate dehydrogenases are compared, the specification does not reasonably provide enablement for a method for improving the thermostability of any protein wherein the amino acid sequences of proteins of different functions are compared (pages 7-9 of paper number 17). Applicants respectfully disagree.

In traverse of this rejection, Applicants submitted the Yamagishi Declaration on June 18, 2003 evidencing the fact that the inventive method may be employed beyond that which is specifically exemplified in the present specification. Applicants wish to thank Examiner Ramirez for acknowledging that “the teachings of the specification (pages 2-3) and Applicant’s declaration in support of the argument that the claimed method can be practiced to improve the thermostability of any protein, it is noted that in the example provided in the specification and that of the declaration, construction of the phylogenic tree and the ancestral protein required the use of proteins from thermophilic bacteria which have functional homologs in non-thermophilic organisms.” (paper number 17, page 8) Consistent with this acknowledged scope, Applicants have amended Claims 17 and 23 (step (i)) to specifically indicate that a phylogenetic tree is constructed by using proteins from thermophilic

organisms. As such, the skilled artisan would readily appreciate this aspect of the claims and how to generate a phylogenetic tree when the present specification is in hand. However, to further assist the artisan, Claims 17 and 23 have been further amended to specify that the phylogenetic tree is constructed by using a limited algorithm (i.e., the maximum parsimony method or the maximal likelihood method).

MPEP § 2164.01 states:

“The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation.”

Applicants submit that one of skill in the art could obtain a protein having improved thermostability, based on the disclosure provided in the specification, without undue experimentation, especially when the disclosure is augmented with the information known in the art.

Further, MPEP § 2164.04 states:

“A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.”

At pages 4-13, the Applicants fully describe the present invention in generic terms so as to enable the artisan to practice the inventive method. Moreover, at pages 13-29, Applicants provide painstaking detail of the inventive method along with a practical example teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented.

Applicants again submit that the method of the present invention may be used with proteins other than those described in the Examples. Specifically, Applicants note that with the present specification in hand “one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation.” (MPEP §2164.01) To support this assertion, Applicants wish to again bring the Examiner’s attention to the following details set forth in the “Summary of the Invention” section of the specification appearing on pages 2-3:

- The method of the present invention does not depend on the particular properties of proteins currently existing.
- The method of the present invention is based on the concept that the ancestors common to eubacteria, eukaryotes and archaeobacteria might be ultra-thermophilic bacteria, after reviewing the fact that many organisms that properly grow at a temperature of 80°C or above are located at the root of a phylogenetic tree by 16S rRNA.
- The inventors have completed the present invention on the basis of an idea that for designing and producing a thermostable protein, it is more important that the amino acid sequence of ancestral protein is estimated and mimicked than that only the sequence and the higher-order structure of protein of a thermophilic bacterium are analyzed and mimicked.

In view of the foregoing and the amendment to Claims 17 and 23 to incorporate that which the Examiner has acknowledged (the use of “proteins from the species selected from the group consisting of thermophilic bacteria and archaeobacteria” in the claimed invention), Applicants submit that the present claims are fully enabled by the specification and the common ability available in the art.

Withdrawal of this ground of rejection is requested.

The rejection of Claims 17-26 under 35 U.S.C. §112, second paragraph, is obviated in part by amendment and traversed in part.

Regarding the Examiner's indefiniteness rejection based on the recitation of "same family." Applicants note that the definition of "proteins belonging to the same family" appears on page 5, line 29 to page 6, line 6 of the present specification and clearly states that this expression includes proteins that are similar to each other in "at least one of the function, amino acid sequence, domain structure, and steric structure." In order to ensure clarity and ease of interpretation, Applicants have amended the claims to add this definition to the claims. Accordingly, the objectionable term is now definite.

The Examiner has also rejected the expression "wherein said proteins evolutionarily correspond to each other in a phylogenic tree" as being indefinite. Applicants note that the specification at page 6, line 24 to page 10, line 25 provide a detailed discussion of how the phylogenetic tree is constructed and, as such, how the proteins correspond to one another on an evolutionary basis.

In one embodiment of the present invention, maximum parsimony method or maximal likelihood method is used for preparing a phylogenetic tree (see page 6, line 26 to page 8, line 14). Accordingly, Claims 17 and 23 have been amended to introduce the limitation of these two methods for preparing a phylogenetic tree. Applicants submit that it is now clear to the skilled artisan that proteins derived from two or more species correspond to each other when these proteins appear at the similar location in the phylogenetic tree designed for each individual species. This fact is also suggested in the specification at page 4, line 20 to page 5, line 2. In addition, the location of the "ancestral protein" in a phylogenetic tree may be found at page 5, lines 10-14, wherein it may be located at the root of the phylogenetic tree.

Based on the foregoing, Applicants submit that the pending claims are definite within the context of 35 U.S.C. §112, second paragraph. Accordingly, Applicants request withdrawal of this ground of rejection.

The objection to the amendment to the specification filed on June 18, 2003 under 35 U.S.C. §132 as introducing new matter and the rejection of Claims 17-26 under 35 U.S.C. §112, first paragraph (new matter), are traversed.

The basis for the Examiner's rejections is the insertion of the limitation "same family" does not find support in the disclosure as originally filed. It is the Examiner's opinion that this limitation constitutes "new matter" and based on this opinion the Examiner has objected to the specification and rejected Claims 17-26. The Examiner attempts to support these rejections by summarily concluding: "The Examiner has not been able to locate support of "proteins belonging to the same family"." Applicants respectfully disagree with this conclusion by the Examiner.

Applicants wish to direct the Examiner's attention to the specification at page 5, lines 7-14, which clearly recites "by comparing the protein with a protein of archaeobacteria or *with another protein of the same family.*" (*emphasis added*) Applicants also wish to direct the Examiner's attention to the definition of "*proteins belonging to the same family*" appearing on page 5, line 29 to page 6, line 6. In view of the foregoing, Applicants submit that this ground of objection and rejection are unfounded and should be withdrawn.

Moreover, Applicants note that this amendment served to clarify what are evolutionarily corresponding to each other. Specifically, the targets that are to be evolutionarily corresponded are not "two or more species" but are the "proteins."

Acknowledgment that the objection to the specification and the rejection of Claims 17-26 has been withdrawn is requested.

The objections to the Abstract, the Drawings, and to Claims 17, 18, 23, and 24 are obviated by the present amendment.

As requested by the Examiner, Applicants submit herewith a substitute Abstract, which is in full compliance with 37 C.F.R. §1.72. Regarding the Drawings, Applicants have amended the specification to insert the sequence identifiers for the sequences disclosed in the figures. Finally, the objectionable Claims have been either cancelled or amended per the Examiner's kind suggestion.

Withdrawal of these grounds of objection is requested.

Applicants submit that the present application is now in condition for allowance. Early notification of such action is earnestly solicited.

Respectfully submitted,

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